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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,625	11/02/2006	Stephen J. Klaus	FP0617 US	7369

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EXAMINER	
OGUNBIYI, OLUWATOSIN A	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,625	KLAUS ET AL.	
	Examiner	Art Unit	
	Oluwatosin Ogunbiyi	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *17,18,34,35,37,38 and 44-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16, 19-33, 36 and 39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-47* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/14/06 and 4/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-47 are pending in the application. Claims 1-16, 19-33, 36 39-43 are under examination. Claims 17,18, 34,35,37,38, 44-47 are withdrawn.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Information Disclosure Statement

The information disclosure statements filed 4/18/06 and 3/14/06 has been considered. Initialed copies are enclosed.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

- Group I, claim(s) 1-36, 39-45 drawn to a method for increasing endogenous gamma globin in a subject, the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globulin and drawn to a method for treating or pretreating a subject infected with or at risk for being infected with a species of Plasmodium, the method comprising increasing fetal hemoglobin level in the subject.

- Group II, claim(s) 37,38,46,47 drawn to a medicament comprising an agent which increases expression of the gene encoding gamma globulin for use in increasing fetal hemoglobin level in a subject.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

- The technical feature of Groups I is a method for increasing endogenous gamma globin in a subject, the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globulin.
- The technical feature of Groups II is a medicament comprising an agent which increases expression of the gene encoding gamma globulin for use in increasing fetal hemoglobin level in a subject.

Group I lacks unity with Group II because the technical feature of Group I is anticipated by the art (Perrine et al, Blood vol. 74 p. 454-459 July 1989) and therefore not "special" within the meaning of PCT Rule 13.2 because it does not provide for a contribution that the claimed invention makes over the art. Perrine et al teaches a method for increasing endogenous gamma globulin in a subject the method comprising administering to the subject sodium butyrate (see abstract, p. 458 columns 1 last bridging paragraph to column 2).

Notice of Possible Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise

require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Species Election

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. The species are as follows:

Group I

1. Type of cell: a) hematopoietic stem cells b) blast-forming unit erythroid (BFU-E).
2. Second therapeutic agent selected from a) hydroxyurea b) butyrate analogs c) 5-azacytidine

3. HIF hydroxylase enzyme selected from (a) EGLN (b)FIH1 (c) PHD4
4. Species of disorder or condition (a) beta-thalassemia and sickle cell syndrome (b) infection with *Plasmodium*

The following claims are generic and deemed to correspond to the species listed above in the following manner: 1, 10, and 11, 13-19, 24-30 and 31-40.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: technical feature linking species is not novel and is not defined over the prior art. Furthermore, the blast-forming unit erythroid (BFU-E) cell is known in the art (Perrine et al Blood vol. 74 p. 454-459 July 1989) and therefore does not define a special technical feature; and the hydroxyurea is also known in the art (Letvin et al, The New England Journal of Medicine, 1984 vol. 310 0. 869-873) and therefore does not define a special technical feature. The HIF hydroxylase enzymes and sickle cell syndromes are known in the art (Klaus et al. WO 03/053997 A2 published 3 July 2003).

Applicant is required, in reply to this action, to elect a single species from each species category numbered 1-4 above to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

As to HIF hydroxylase enzymes, if Applicant elects EGLN then EGLN1, EGLN2 and EGLN3 will all be examined.

As to species of disorder, both beta-thalassemia and sickle cell syndrome will be examined together if they are elected.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include

all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Christopher Turner on 12/7/07 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-36 and 39-45 and the species hematopoietic stem cells, hydroxyurea, EGLN and beta-thalassemia and sickle cell syndrome. Affirmation of this election must be made by applicant in replying to this Office action. Claims 17,18, 34,35,37,38, 44-47

are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-16, 19-21, 23-27, 39-43 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1-16, 17-24, 27-3, 34-54, of copending Application No.11/348294 ('294) . This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The claims of the instant invention and that of the '294 application are both drawn to a method for increasing endogenous gamma globin in a subject, the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 39-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39-43 provides for the use of the medicament of claim 37, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 11 is drawn to a method for treating a disorder associated with abnormal hemoglobin in a subject, the method comprising increasing the level of fetal hemoglobin in the subject. The claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. The recitation of 'increasing the level of fetal hemoglobin" is not a proper method step.

Claim Rejections - 35 USC § 101

Claims 11 and 39-43 are rejected under 35 U.S.C. 101 because the claimed recitation of a use (claims 39-43) or recitation of an end result of a method step (claim 11), without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 10, 11-16, 19-21, 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Tung et al. WO 97/12855 April 10, 1997.

The claims are drawn to a method for increasing endogenous gamma globin in a subject, the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin.

Tung et al teaches a method for increasing endogenous gamma globin and fetal hemoglobin in a patient (in vivo, humans), the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin (p.1 lines 1-15, p.2 lines 24-33, p. 3, p. 5 lines 16-24). Tung et al teaches a method for treating disorders associated with abnormal hemoglobin such as those which comprise an alteration in the level, structural integrity or activity of adult hemoglobin e. g. beta thalassemia and sickle cell syndromes such as sickle cell trait (sickling) by comprising increasing the level of fetal hemoglobin in a subject (p. 5 lines 16-28). Tung et al teaches that said agent causes the increase in the expression of gamma globin thus fetal hemoglobin. Therefore, when said agent is administered to the subject the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by cells of said subject will increase. Tung et al teaches that the agent is administered in combination

with a second therapeutic agent such as hydroxyurea (p. 24 lines 4-14). Tung et al performs efficacy studies of said method in monkeys (primate) (p. 33 example 5). Tung administers said agent to a subject and thus the cells of said subject as said agent acts at the cellular level by increasing gamma globin in the cells of said subject.

Claims 1, 10, 11-16 and 21-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Perrine et al WO 93/18671 September 30, 1993.

The claims are drawn to a method for increasing endogenous gamma globin in a subject, the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin.

Perrine et al teaches a method for increasing endogenous gamma globin and fetal hemoglobin in a patient (in vivo, humans, primates), the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin (p. 2 lines 25-26, p. 6 lines 5-8 p. 9 example 4 and 5). Perrine et al teaches a method for treating disorders associated with abnormal hemoglobin such as those which comprise an alteration in the level, structural integrity or activity of adult hemoglobin e. g. beta thalassemia and sickle cell syndromes such as sickle cell trait sickle - cell anemia and beta thalassemia, hemoglobin beta 0 or + thalassemia, comprising increasing the level of fetal hemoglobin in a subject (p. 2 lines 9-24)). Perrine et al teaches that said agent causes the increase in the expression of gamma globin thus fetal hemoglobin (example 4 and 5). Therefore, when said agent is administered to the subject the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by cells of said subject will increase. Perrine et al administers said agent to cells from erythroid progenitors from peripheral blood from patients having a betaglobin disorder, thus Perrine administers said agent ex vivo (p. 4 example 4). Perrine et al administers said agent to a subject and thus the cells of said subject as said agent acts at the cellular level by increasing gamma globin in the cells of said subject. Erythroid progenitors are produced by bone marrow cells thus Perrine administers said agent to cells derived from the bone marrow.

Claims 1, 10, 11-16, 21-33 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Bohmer et al WO 01/12784 A1 22 February 2001.

The claims are drawn to a method for increasing endogenous gamma globin and fetal hemoglobin in a subject, the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin.

Bohmer et al teaches a method for increasing endogenous gamma globin and fetal hemoglobin in a patient (in vivo, humans, primates), the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin (see abstract, p. 8 lines 1-14, p. 9 example 1 lines12-15). Bohmer monitors an increase in the level of fetal hemoglobin or HbF by using antibodies to the gamma globin chain of HbF (p. 9 example 1).

Bohmer et al teaches a method for treating disorders associated with abnormal hemoglobin such as those which comprise an alteration in the level, structural integrity or activity of adult hemoglobin e. g. beta thalassemia and sickle cell syndromes such as sickle cell trait (sickled hemoglobin), sickle cell anemia and beta thalassemia comprising increasing the level of fetal hemoglobin in a subject (see abstract, p. 2 lines 10- 25)

Bohmer et al teaches that said agent causes the increase in the expression of gamma globin thus increased levels of fetal hemoglobin as exemplified by the monitoring of the levels of gamma globin present in fetal hemoglobin (9 example 1, fig. 1). Therefore, when said agent is administered to the subject the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by cells of said subject will increase. Bohmer et al administers said agent in vivo or ex vivo (abstract, p. 17 and 18 claims 1 and 15).

Bohmer et al administers said agent to cells derived from bone marrow such as hematopoietic stem cells (Claim 1 and 5 p. 17).

Bohmer et al teaches am method for increasing the level of fetal hemoglobin in a subject having abnormal hemoglobin such as beta thalassemia and sickle cell syndrome such as sickle cell trait and sickle cell anemia comprising administering to a population of cells (such as hematopoietic stem cells) an agent which increase the number of fetal hemoglobin producing cells (resulting from increased expression of the

gene encoding gamma globin) and transferring said cells into the subject (p. 2 lines 10-25, p. 17 claim 1, 5).

Claims 1-16, 19, and 21-25 are rejected under 35 U.S.C. 102(a) as being anticipated by Klaus et al. WO 03/053997 A2 published 3 July 2003 as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293

The claims are drawn to a method for increasing endogenous gamma globin and fetal hemoglobin in a subject, the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin.

Klaus teaches a method for increasing endogenous erythropoietin in vitro and in vivo by administering a compound which/agent which increase endogenous erythropoietin (see abstract, see p. 3 paragraph 14). Erythropoietin increases expression of the gene encoding gamma globin thus increasing the level of fetal hemoglobin as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293 (see first sentence of abstract and first paragraph of the introduction). Thus, said method of increasing endogenous erythropoietin of Klaus et al will increase endogenous gamma globin and thus increase fetal hemoglobin absent evidence to the contrary. Said agent of Klaus et al which increases endogenous erythropoietin thus endogenous gamma globin increases the stability or activity of the alpha subunit of hypoxia inducible factor alpha (HIF1, HIF2 and HIF3 and any fragment thereof) by inhibiting hydroxylation of said HIF alpha endogenous to said subject (p.3 paragraphs 9-12). Further, Klaus et al teaches a method for increasing endogenous erythropoietin thus increasing expression of the gamma globin gene by administering an agent which inhibits 2-oxoglutarate dioxygenase enzyme activity such as enzyme activity of EGLN1, EGLN2, EGLN3 or any subunit or fragment thereof or inhibits HIF hydroxylase enzyme activity of HIF hydroxylase enzymes such as EGLN1, EGLN2, EGLN3 (p. 3 paragraph 13).

Klaus et teaches said method (which inherently increases fetal hemoglobin as set forth supra) to treat disorders associated with abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 22 paragraph 45 and 460. Said method would result in

the increased proportion of fetal hemoglobin producing cells to non-fetal hemoglobin producing cells as erythropoietin acts as the cellular level by increasing gamma gene expression, thus increasing fetal hemoglobin. Said agent of Klaus et al is administered with a second therapeutic agent such as exogenous erythropoietin or G-CSF (p.19 paragraph 30). The method of Klaus et al is performed in vivo or ex vivo (in vitro) (abstract) and the agent is administered to primates e.g. humans or a cell(p. 3 paragraph 10).

Status of the Claims

Claims 1-16, 19-33, 36, 39-43 are rejected. Claims 17,18, 34,35,37,38, 44-47 are withdrawn. No claims allowed.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Tosin Ogunbiyi

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